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TITLE: B7-like molecules and uses thereof

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CLAIMS:

What is claimed is:

1. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of: (a) the nucleotide sequence as set forth in SEQ ID NO: 1; (b) a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NO: 2; (c) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of either (b) or (c); and (d) a nucleotide sequence complementary to either (b) or (c).

2. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of: (a) a nucleotide sequence encoding a polypeptide which is at least about 70 percent identical to the polypeptide as set forth in SEQ ID NO: 2, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2; (b) a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in SEQ ID NO: 1 or (a); (c) a region of the nucleotide sequence of SEQ ID NO: 1, (a), or (b) encoding a polypeptide fragment of at least about 25 amino acid residues, wherein the polypeptide fragment has an activity of the encoded polypeptide as set forth in SEQ ID NO: 2, or is antigenic; (d) a region of the nucleotide sequence of SEQ ID NO: 1 or any of (a)-(c) comprising a fragment of at least about 16 nucleotides; (e) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of any of (a)-(d); and (f) a nucleotide sequence complementary to any of (a)-(d).

3. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of: (a) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2; (b) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one amino acid insertion, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2; (c) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one amino acid deletion, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2; (d) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 which has a C- and/or N-terminal truncation, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2; (e) a

nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one modification selected from the group consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-terminal truncation, and N-terminal truncation, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2; (f) a nucleotide sequence of any of (a)-(e) comprising a fragment of at least about 16 nucleotides; (g) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of any of (a)-(f); and (h) a nucleotide sequence complementary to any of (a)-(e).

4. A vector comprising the nucleic acid molecule of any of claims 1, 2, or 3.

5. A host cell comprising the vector of claim 4.

6. The host cell of claim 5 that is a eukaryotic cell.

7. The host cell of claim 5 that is a prokaryotic cell.

8. A process of producing a B7-L polypeptide comprising culturing the host cell of claim 5 under suitable conditions to express the polypeptide, and optionally isolating the polypeptide from the culture.

9. A polypeptide produced by the process of claim 8.

10. The process of claim 8, wherein the nucleic acid molecule comprises promoter DNA other than the promoter DNA for the native B7-L polypeptide operatively linked to the DNA encoding the B7-L polypeptide.

11. The isolated nucleic acid molecule according to claim 2, wherein the percent identity is determined using a computer program selected from the group consisting of GAP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, and the Smith-Waterman algorithm.

12. A process for determining whether a compound inhibits B7-L polypeptide activity or B7-L polypeptide production comprising exposing a cell according to any of claims 5, 6, or 7 to the compound and measuring B7-L polypeptide activity or B7-L polypeptide production in said cell.

13. An isolated polypeptide comprising the amino acid sequence as set forth in SEQ ID NO: 2.

14. An isolated polypeptide comprising the amino acid sequence selected from the group consisting of: (a) the amino acid sequence as set forth in SEQ ID NO: 3, optionally further comprising an amino-terminal methionine; (b) an amino acid sequence for an ortholog of SEQ ID NO: 2; (c) an amino acid sequence which is at least about 70 percent identical to the amino acid sequence of SEQ ID NO: 2, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2; (d) a fragment of the amino acid sequence set forth in SEQ ID NO: 2 comprising at least about 25 amino acid residues, wherein the fragment has an activity of the polypeptide set forth in SEQ ID NO: 2, or is antigenic; and (e) an amino acid sequence for an allelic variant or splice variant of the amino acid sequence as set forth in SEQ ID NO: 2 or any of (a)-(c).

15. An isolated polypeptide comprising the amino acid sequence selected from the group consisting of: (a) the amino acid sequence as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2; (b) the amino acid sequence as set forth in SEQ ID NO: 2 with at least one amino acid insertion, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2; (c) the amino acid sequence as set forth in SEQ ID NO: 2 with at least one amino acid deletion, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2; (d) the amino acid sequence as set forth in SEQ ID NO: 2 which has a C- and/or N-terminal truncation, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2; and (e) the amino acid sequence as set forth in SEQ ID NO: 2 with at least one modification selected from the group consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-terminal truncation, and N-terminal truncation, wherein the polypeptide has an activity of

the polypeptide set forth in SEQ ID NO: 2.

16. An isolated polypeptide encoded by the nucleic acid molecule of any of claims 1, 2, or 3, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2.

17. The isolated polypeptide according to claim 14, wherein the percent identity is determined using a computer program selected from the group consisting of GAP, BLASTP, FASTA, BLASTA, BLASTX, BestFit, and the Smith-Waterman algorithm.

18. A selective binding agent or fragment thereof that specifically binds the polypeptide of any of claims 13, 14, or 15.

19. The selective binding agent or fragment thereof of claim 18 that specifically binds the polypeptide comprising the amino acid sequence as set forth in SEQ ID NO: 2, or a fragment thereof.

20. The selective binding agent of claim 18 that is an antibody or fragment thereof.

21. The selective binding agent of claim 18 that is a humanized antibody.

22. The selective binding agent of claim 18 that is a human antibody or fragment thereof.

23. The selective binding agent of claim 18 that is a polyclonal antibody or fragment thereof.

24. The selective binding agent claim 18 that is a monoclonal antibody or fragment thereof.

25. The selective binding agent of claim 18 that is a chimeric antibody or fragment thereof.

26. The selective binding agent of claim 18 that is a CDR-grafted antibody or fragment thereof.

27. The selective binding agent of claim 18 that is an antiidiotypic antibody or fragment thereof.

28. The selective binding agent of claim 18 that is a variable region fragment.

29. The variable region fragment of claim 28 that is a Fab or a Fab' fragment.

30. A selective binding agent or fragment thereof comprising at least one complementarity determining region with specificity for a polypeptide having the amino acid sequence of SEQ ID NO: 2.

31. The selective binding agent of claim 18 that is bound to a detectable label.

32. The selective binding agent of claim 18 that antagonizes B7-L polypeptide biological activity.

33. A method for treating, preventing, or ameliorating a B7-L polypeptide-related disease, condition, or disorder comprising administering to a patient an effective amount of a selective binding agent according to claim 18.

34. A selective binding agent produced by immunizing an animal with a polypeptide comprising an amino acid sequence of SEQ ID NO: 2.

35. A hybridoma that produces a selective binding agent capable of binding a polypeptide according to any of claims 1, 2, or 3.

36. A method of detecting or quantitating the amount of B7-L polypeptide using the anti-B7-L antibody or fragment of claim 18.

37. A composition comprising the polypeptide of any of claims 13, 14, or 15, and a pharmaceutically acceptable formulation agent.
38. The composition of claim 37, wherein the pharmaceutically acceptable formulation agent is a carrier, adjuvant, solubilizer, stabilizer, or anti-oxidant.
39. The composition of claim 37 wherein the polypeptide comprises the amino acid sequence as set forth in SEQ ID NO: 3.
40. A polypeptide comprising a derivative of the polypeptide of any of claims 13, 14, or 15.
41. The polypeptide of claim 40 that is covalently modified with a water-soluble polymer.
42. The polypeptide of claim 41, wherein the water-soluble polymer is selected from the group consisting of polyethylene glycol, monomethoxy-polyethylene glycol, dextran, cellulose, poly-(N-vinyl pyrrolidone) polyethylene glycol, propylene glycol homopolymers, polypropylene oxide/ethylene oxide co-polymers, polyoxyethylated polyols, and polyvinyl alcohol.
43. A composition comprising a nucleic acid molecule of any of claims 1, 2, or 3 and a pharmaceutically acceptable formulation agent.
44. The composition of claim 43, wherein said nucleic acid molecule is contained in a viral vector.
45. A viral vector comprising a nucleic acid molecule of any of claims 1, 2, or 3.
46. A fusion polypeptide comprising the polypeptide of any of claims 13, 14, or 15 fused to a heterologous amino acid sequence.
47. The fusion polypeptide of claim 46, wherein the heterologous amino acid sequence is an IgG constant domain or fragment thereof.
48. A method for treating, preventing, or ameliorating a medical condition comprising administering to a patient the polypeptide of any of claims 13, 14, or 15, or the polypeptide encoded by the nucleic acid of any of claims 1, 2, or 3.
49. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising: (a) determining the presence or amount of expression of the polypeptide of any of claims 13, 14, or 15, or the polypeptide encoded by the nucleic acid molecule of any of claims 1, 2, or 3 in a sample; and (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.
50. A device, comprising: (a) a membrane suitable for implantation; and (b) cells encapsulated within said membrane, wherein said cells secrete a protein of any of claims 13, 14, or 15; and said membrane is permeable to said protein and impermeable to materials detrimental to said cells.
51. A method of identifying a compound which binds to a B7-L polypeptide comprising: (a) contacting the polypeptide of any of claims 13, 14, or 15 with a compound; and (b) determining the extent of binding of the B7-L polypeptide to the compound.
52. The method of claim 51, further comprising determining the activity of the polypeptide when bound to the compound.
53. A method of modulating levels of a polypeptide in an animal comprising administering to the animal the nucleic acid molecule of any of claims 1, 2, or 3.
54. A transgenic non-human mammal comprising the nucleic acid molecule of any of claims 1, 2, or 3.

55. A process for determining whether a compound inhibits B7-L polypeptide activity or B7-L polypeptide production comprising exposing a transgenic mammal according to claim 54 to the compound, and measuring B7-L polypeptide activity or B7-L polypeptide production in said mammal.
56. A nucleic acid molecule of any of claims 1, 2, or 3 attached to a solid support.
57. An array of nucleic acid molecules comprising at least one nucleic acid molecule of any of claims 1, 2, or 3.
58. An isolated polypeptide comprising the amino acid sequence as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution selected from the group consisting of: methionine at position 4; leucine or methionine at position 12; leucine or valine at position 13; leucine or valine at position 16; leucine or valine at position 17; leucine, valine, or methionine at position 18; leucine or valine at position 23; leucine at position 26; leucine or valine at position 27; valine or leucine at position 31; leucine or isoleucine at position 39; alanine at position 46; valine at position 48; alanine at position 52; isoleucine at position 54; glutamic acid at position 61; valine at position 64; glutamic acid at position 66; leucine, methionine, or valine at position 67; valine or leucine at position 69; arginine at position 73; leucine at position 76; valine at position 79; methionine at position 80; tyrosine at position 83; arginine at position 84; aspartic acid at position 85; arginine at position 87; glutamic acid at position 88; aspartic acid at position 92; tyrosine at position 97; lysine at position 98; leucine, isoleucine, or methionine at position 103; isoleucine, leucine, or methionine at position 108; isoleucine at position 115; isoleucine at position 117; leucine or isoleucine at position 120; valine or isoleucine at position 122; serine at position 123; glutamic acid at position 124; serine at position 127; phenylalanine at position 128; arginine at position 129; phenylalanine at position 131; valine at position 132; alanine at position 137; valine or isoleucine at position 143; alanine at position 148; glycine at position 149; isoleucine or methionine at position 155; isoleucine or methionine at position 157; isoleucine at position 166; tyrosine at position 174; isoleucine, leucine, or methionine at position 179; isoleucine at position 180; leucine at position 194; phenylalanine at position 215; serine at position 218; serine at position 222; isoleucine or leucine at position 226; valine or leucine at position 227; leucine or valine at position 231; isoleucine at position 240; aspartic acid at position 242; methionine or leucine at position 245; arginine at position 246; threonine at position 256; valine or isoleucine at position 260; leucine or isoleucine at position 262; leucine or valine at position 268; valine or methionine at position 272; valine at position 273; valine, isoleucine, or methionine at position 275; phenylalanine at position 278; valine or isoleucine at position 279; isoleucine or valine at position 281; and arginine at position 282; wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2.